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Original Article

Emerging perspectives in prostate cancer: Insights from the 4th Asia Pacific Prostate Cancer Conference☆

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1. Preamble

The emergence of multiple novel agents targeting distinct pathways in the last several years have caused a paradigm shift in the management of advanced prostate cancer. With evidence of clinically meaningful efficacy, these agents when coupled with proper sequencing and used in a multidisciplinary care setting could provide patients with better survival whilst maintaining good quality of life.

2. The changing paradigms in prostate cancer

Prostate cancer is the main cause of cancer-related mortality among men. And although surgery and radiation have been successful treatments, between 30% and 40% of prostate cancer patients progress to advanced forms of the disease.[1] Almost all patients with metastatic prostate cancer go on to develop castration-resistant prostate cancer (CRPC).[2]

From 2004 to 2010, docetaxel-based chemotherapy was the only approved agent for the treatment of metastatic CRPC.[3,4] Nevertheless, significant advances in the understanding of the androgen pathway role over the last decade have led to the development of alternative novel hormonal agents such as abiraterone and enzalutamide to treat advanced castration-resistant prostate cancer. Both agents target the androgen axis but with distinct mechanisms of action. Abiraterone inhibits the synthesis of androgen by blocking cytochrome P450 17, while enzalutamide inhibits the androgen receptor.[5] Furthermore, the identification of high-risk germ-line mutations such as BRCA2, and now evidence for somatic aberration in these DNA damage response pathways, is opening up further treatment options in mCRPC.

With this increase in knowledge, therapeutic options for patients are expanding leading to improvements in overall survival,[3] significantly changing the standard of care for the disease. These innovations in understanding the molecular evolution of mCRPC could potentially provide physicians the ability to do targeted screening of patients at risk as well as stratify patients according to molecular subtypes for different management strategies.[6]

Despite this major development in the field, androgen deprivation therapy (ADT) remains the backbone treatment for advanced prostate cancer.

3. Novel agents as systemic treatments

Metastatic prostate cancer and CRPC can be managed with a range of treatments including secondary hormonal therapies, which are associated with good outcomes when used in combination with ADT. Treatments for patients are chosen based on prior therapy, symptom burden, type of metastases, performance status, comorbidities, adverse event profiles, patient preference, and treatment sequence.[5]

Treatment sequencing is an important consideration as some agents can affect a patient's responses to subsequent therapeutic strategies,[5] as well as the achievement of prolonged remissions.[7] With the emergence of novel agents, the next stage in research will be to determine appropriate and cost-effective ways of sequencing available agents to provide patients with greater benefit, as well as to validate biomarkers that select agents that elicit the best response in individual patients.

Novel AR-directed therapies have demonstrated improved overall survival in metastatic CRPC patients.[5] Some of these novel agents have shown promising results when used earlier in the natural history of the disease and have the potential to radically alter the current treatment pathway paradigms. Patients with metastatic CRPC who were symptomatic or mildly symptomatic

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chemotherapy-naïve on abiraterone and prednisone had longer overall survival compared with patients on placebo plus prednisone.[8] Enzalutamide also provided improved overall survival outcomes for the same type of patient populations compared to placebo.[9]

Within the US setting, abiraterone does not appear to significantly impact healthcare cost allocation due to the small number of patients eligible for treatment and the lower incidences of toxicity compared to chemotherapy.[10–12] Nevertheless, a better understanding of the benefits of these costly novel treatments in association to its full cost which include the cost of treating adverse events is needed.

4. A collaborative approach to disease management

As treatment for prostate cancer should be specific to the patient and his specific cancer,[13] the involvement of a multidisciplinary team involving the urologist, (molecular) oncologist, (molecular) pathologist, and radiologist is recommended.[14] The adoption of multidisciplinary teams have increased worldwide, and this strategy has benefited both patients and healthcare professionals.[15] In one study, patients on the multidisciplinary arm had similar outcomes as patients on the standard evaluation despite having higher-risk disease.[16] The same study also found that a multidisciplinary approach did not cause delay in time to radical prostatectomy.[16] Nevertheless, as this approach could be time consuming and resource intensive, prioritising cases by disease complexity, tumour type, or the availability of members could be a feasible way of incorporating it into patient care.[15] Another study has also shown that weekly evaluations with the different specialists doing patient consultations, going through the data, and discussing management strategies within a single day to be practical.[17]

5. The 4th Asia Pacific Prostate Cancer Conference

In view of the evolving paradigms in prostate cancer management, particularly with the advent of novel therapeutic agents, it is important to provide a platform to debate current data. The 4th Asia Pacific Prostate Cancer Conference is a forum for regional urologists and oncologists with a special interest in the management of prostate cancer to discuss the applicability of such data in day-to-day practice.

Building on the success of conferences past, the theme of this year's Asia Pacific Prostate Cancer Conference was *Emerging Perspectives in Prostate Cancer (EPiC)*. Hosted by the Academy for Cancer Education (ACE) and endorsed by the Asia Pacific Prostate Society (APPS) as well as the Asia Pacific Society of Uro-Oncology (APSU), this meeting is becoming one of the important medical educational meetings for clinicians involved in the treatment of advanced prostate cancer in this region. For the fourth time, the conference served as a timely platform for valuable exchanges between prostate cancer care providers from different specialties practising in either reimbursed or self-pay healthcare systems. The Japanese health system, for example, delivers one of the largest universal coverage in Asia Pacific and has been providing significant subsidy and access of novel agents to CRPC patients.

This EPiC meeting provided an overview of the latest clinical data and pharmacoeconomic principles within the context of advanced prostate cancer. The participants deliberated on updated data and practice principles in relation to real-world resource-stratified practices in the Asia Pacific. A steering committee of experts was convened in August 2014 to guide the development of this year's meeting agenda. This ensured that the scientific content of this meeting were driven by the educational needs of clinicians in the region. The conference showcased an impressive faculty of 20 highly sought after regional key opinion leaders and included didactic lectures, case study presentations, debates on pertinent topics as well as open panel conversations with the faculty.

The meeting was also an avenue for cross-country and multidisciplinary interactions among clinicians across Asia Pacific, with the participation of 172 delegates from 12 countries (Australia, China, Hong Kong, Indonesia, India, Japan, Malaysia, Singapore, South Korea, Taiwan, Thailand, and Vietnam). As host, Japan comprised 63% of the audience. Majority of the participants were urologists (91%), and the rest were oncologists. Most of them served in the public sector (80%). In addition, the debates and case study sessions were broadcasted live to 19 sites across India, Nepal and Bangladesh; reaching in excess of 160 urologist and oncologist viewers. Viewers were able to make comments and questions in real time. Selected questions were also addressed live by the panel of experts at the conference.

The abstracts of presentations at the 4th Asia Pacific Prostate Cancer Conference could be found in this supplement.

6. Prostate care management practices in Asia Pacific: Findings of a pre-meeting survey

One hundred and eighteen participants from countries represented at the 4th Asia Pacific Prostate Cancer Conference responded to the survey. As almost a quarter of the respondents (37%) were Japanese delegates, the results from the individual countries other than Japan are limited by small sample sizes. Majority of the respondents worked in the public sector (73%) and were urologists (82%). Seventy percent had more than 10 years of experience in treating prostate cancer.

According to the responses, the majority (78%) indicated that CRPC comes under the care of the urologist in their respective countries; only 19% indicated that oncologists were primarily responsible for the care of CRPC patients. A small number (2%) indicated both specialties were responsible.

Participants indicated that the main reason for the increasing incidence of prostate cancer in the countries was the ageing population. Other major factors were the increase in demand for testing and screening as well as heightened disease awareness.

In the pre-meeting survey, delegates were also given patient scenarios to consider. For a patient with 10 years life expectancy and intermediate risk for localised prostate cancer (Gleason score of 7), 34% of respondents indicated that they would opt for robotic radical prostatectomy as first-line therapy. 27% chose radical radiotherapy, with or without ADT, and 14% chose laparoscopic radical prostatectomy. Stratification by countries revealed differences in practices across the region. Robotic radical prostatectomy was the main treatment of choice for these types of patients in Japan, Singapore, and Taiwan; but not so in Thailand, Vietnam, and China.

This difference between countries in the Asia Pacific region is also seen in terms of the therapies reimbursed by the government healthcare system. Singapore had the most number of therapies approved while Vietnam had the least number of therapies reimbursed. In terms of novel agents for the treatment of prostate cancer, abiraterone was approved in all countries surveyed and reimbursed in Japan for all CRPC patients and in Taiwan for some CRPC patients. Whereas enzalutamide was approved in Singapore and Japan, it was under filing in Taiwan, Vietnam and Indonesia, and undergoing clinical trial in China.

Forty two percent of respondents would not consider first-line adjuvant chemotherapy for all patients with hormone-sensitive metastatic prostate cancer but more than half would opt for this only if the patients had a heavy burden of metastases. The survey revealed that clinicians in Taiwan and Singapore mainly reserved adjuvant chemotherapy for patients with a heavy burden of metastases. In Japan and Thailand, more than half would never consider the treatment for hormone-sensitive patients. In Vietnam, half of the respondents would not consider it, while the other half would use it for all hormone-sensitive patients.

The majority of the respondents (75%) would use a combination of prostate-specific antigen (PSA) tests, imaging, and clinical symptoms to diagnose progression of prostate cancer in their practices. Twenty three percent would only base their diagnosis on PSA test results. A small number of physicians from Japan and Thailand used imaging. Forty percent of physicians would diagnose a patient with CRPC when he fails combined androgen blockade (CAB). This was specifically the approach in Singapore and Japan. At least half of the physicians in Thailand, Taiwan, and Vietnam would diagnose a patient with CRPC if he failed luteinising hormone-releasing hormone (LHRH) or gonadotropin-releasing hormone (GnRH).

The majority (81%) of the physicians were aware that prostate cancer cells create androgen to grow themselves. Many were also familiar with other CRPC mechanisms.

Forty four percent would use docetaxel plus prednisone as first-line treatment for symptomatic metastatic CRPC, while 20% would use abiraterone plus prednisone, and 17% would opt for ADT. Analysed by country, the survey results show that Thailand had the highest number of physicians (44%) who would consider using abiraterone plus prednisone first-line, while in Taiwan, only 8% of the physicians would consider the combination as first-line due to its reimbursement policy for post-chemo usage.

When asked about the various approaches used to treat symptomatic bone metastases in patients with metastatic CRPC, more physicians (66%) would provide palliative care in a post-chemotherapy setting than in the pre-chemotherapy setting (42%). This trend was seen in all countries except in Taiwan and Thailand. In Taiwan, although less than half of the physicians would provide palliative care for patients in either setting, slightly more physicians would provide palliative care before chemotherapy than after. In Thailand, 71% of physicians would provide palliative care in both settings. The biggest disparity in the provision of palliative care services between pre- and post-chemotherapy settings were seen in Japan (28% vs. 72%).

Finally, when asked about their approach when a symptomatic, mCRPC patient with good performance status and prior docetaxel chemotherapy refuses treatment that is expected to produce good treatment outcomes due to high medical costs, 62% would try to persuade the patient to receive the treatment if he has more than 10 years life expectancy. If the patient is expected to live for less than 10 years, 35% would treat with a cheaper existing agent while expecting poorer outcomes and 31% would offer palliative care. Nevertheless, 28% would still persuade the patient to try for the better treatment option. Life expectancy appears to be an important determinant for treatment in Japan. Three-in-four Japanese urologist or oncologist would persuade patients with a 'long life expectancy' (>10 years) to receive the treatment associated that conferred 'better outcomes' even if it was the more expensive treatment. Only 27% would do so if the patients had a 'short life expectancy' (<10 years). Interestingly, despite having universal healthcare coverage in the country, Japan also had the most number of physicians willing to treat with cheaper drugs if the patient had a short life expectancy than all other countries. If the patient has many more years to live, however, Japanese physicians were less likely than physicians from other countries to use the cheaper agent. In self-pay healthcare systems such as Singapore and Thailand, physicians would try to persuade patients to receive the treatment associated with 'better outcomes' in spite of financial constraints. In Vietnam, only 30 – 33% of the physicians would persuade the patient to receive the higher costing treatment even if it was associated with 'better outcomes', regardless of the patient's life expectancy.

It should be noted that these results were obtained from a pre-meeting survey conducted prior to the 4th Asia Pacific Prostate Cancer Conference. The results provide a snapshot of management practices of participants from across Asia Pacific countries represented at the conference; and interestingly contrast with some of the results from the 1st APCCC in St. Gallen, which involved 41 panelists mainly from the US and EU, who made recommendations for advanced prostate cancer.[18] These findings also do not represent management practices of all clinicians within specific countries across the region.

Conflicts of interest

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